REMARKS

The specification has been amended to remove embedded hyperlinks and to correct clerical errors. Support for the changes on page 8 are found on page 36, lines 7 through 10. It is believed that no new matter has been added.

Claims 14-24, 29, and 31-33 are currently pending with Claim 14 being the sole independent claim.

Claims 1 and 25 have been canceled.

Claim 14 was amended to clarify the complement of the polynucleotide of the invention to be the full complement. Support for this amendment can be found in the specification on page 13 of the specification at lines 3-20. Thus, no new matter has been added. Claim 14 now also recited the Clustal alignment method with default parameters. Support for this can be found on page 10 at lines 29-33. Thus, no new matter has been added.

Claims 31 and 32 were amended to read "the transformed plant cells of step (a)". Support for this amendment can be found in the specification on page 17 at lines 10-25 and elsewhere in the specification. It is believed that no new matter has been added.

Claim 33 was clarified to read "the recombinant DNA construct of Claim 19". Support for this can be found in the specification and the claims as originally filed. It is believed that no new matter has been added.

Claims 1, 14-25, 29, 31-33 were rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. It is stated on page 4 of the Office Action that Applicants "claim the recited nucleic acid sequences by functional characteristics without presenting any functional motifs which characterize the biological activities of MS genes. Without a correlation between structure and function or an identification of relevant identifying characteristics conserved in MS genes, it is unclear how the skilled artisan would identify additional members of the claimed genus. . . ."

Submitted herewith is Appendix A which sets forth a Clustal V alignment of the amino acid sequences set forth in SEQ ID NOs:2, 4, and 6 of the instant application with the cobalamin independent methionine synthases from *E. coli* (NCBI gi No. 836660), *Catharanthus roseus* (NCBI gi No. 1362086), *Coleus blumei* (amino acids 21-84, NCBI gi No. 974782), *Arabidopsis thaliana* (NCBI gi No. 2738248), *Mesembryanthemum crystallinum* (NCBI gi No. 1814403), Arabidopsis thaliana

(NCBI gi No), and *Solanum tuberosum* (NCBI gi No. 8339545). Amino acids conserved among all the sequences are indicated by an asterisk (*) below the alignment and those conserved only among the plant sequences are indicated by a plus sign (+). The conserved domain containing the active site cysteine (corresponding to E. coli 726) is shown boxed. This alignment shows that the cobalamin independent methionine synthases to be highly conserved. At least 7 domains containing at least 9 amino acids are 100% conserved among the bacterial and plant Methionine synthases.

In view of this alignment, it is respectfully submitted that the methionine synthase amino acid sequences are highly conserved, and that the amino acids previously identified as being essential for activity are conserved in the plant and bacterial methionine synthases.

Thus, since the amino acid sequences set forth in SEQ ID NOs:2 and 4 possess these conserved domains, one skilled in the art would expect these polypeptides to possess methionine synthase activity.

Furthermore, Ravanel et al. (1998, Proc. Natl. Acad. Sci. U.S.A., previously submitted) state on page 7808, right hand column, first full paragraph, that " [a]mino acid sequences deduced from the plant cDNAs are highly conserved among themselves (>80% identity) and show near 50% identity with the cobalamin-independent methionine synthase from *E. coli*."

To reiterate, one skilled in the art would expect the instant polypeptides to possess methionine synthase activity.

Accordingly, withdrawal of the rejection of the claims under under 35 USC §112, first paragraph, as failing to comply with the written description requirement is respectfully requested.

Claims 14-25 and 31-33 were rejected under 35 USC §112, first paragraph, on the ground that one skilled in the art would need to engage in undue experimentation in order to make and use the claimed invention.

The following is noted with respect to the Forman/Wands factors discussed on pages 6-8 of the Office Action:

1) Unpredictability of the art

Reliance on Eichel et al., 1995, is misplaced since the focus of the Eichel article was the molecular characterization, regulation, heterologous expression and enzyme properties of methionine synthase.

Attention is kindly invited to Zeh et al., Plant Molecular Biology 48:255-265 (2002) (copy enclosed) which states on page 256 that "[m]ethionine synthases have been investigated biochemically and several genes have been clones recently. Most data have been obtained with partially purified enzymes and recombinant proteins (Cossins, 1980; Madison, 1990, Eichel et al., 1995; Eckermann et al., 2000). . . . Genes encoding methionine synthases have been isolated from different organisms. For higher plants, full-length cDNAs were reported for *Catharanthus roseus* (Eichel et al., 1995;X83499), *Chlamydomonas reinhardtii* (Kurvavi et al., 1995; U36197), *Chlamydomonas moewusii* (U77388) and *Coleus blumei* (Peterson et al., 1995; Z49150) or published in the database for *Arabidopsis thaliana* (Gakiere et la., 1999; U97200) and *Mesembryanthemum crystallinum* (U84889)."

It is respectfully submitted that one skilled in the art could readily obtain sequences encoding MS as evidenced by the aforementioned articles without engaging in undue experimentation.

With respect to the comment on page 7, that a method of **identifying** a sequence within the confines of the claimed subject matter does not constitute a method of **making** the sequences, it might be helpful to start with the definition of the the verb "make." What does it mean to "make" something? The following was obtained from Miriam Webster's on-line dictionary:

Main Entry: [1]**make**
Pronunciation: 'mAk
Function: *verb*
Inflected Form(s): **made** /'mAd/; **mak·ing**
Etymology: Middle English, from Old English *macian;* akin to Old High German *mahhOn* to prepare, make, Greek *magEnai* to be kneaded, Old Church Slavonic *mazati* to anoint, smear
transitive senses . . .
3 a : **to bring into being by forming, shaping, or altering material : FASHION** <*make* a dress> **b : COMPOSE, WRITE** <*make* verses> **c :** to lay out and construct <*make* a road> . . . . (Emphasis added).

Thus, one of the definitions of make is "to bring into being by forming, shaping, or altering material." In the context of the instant invention, isolation of plant MS

genes from a variety of plants as described in Example 1 of the instant application, constitutes "making", in that, the MS genes are obtained in a form free of other cellular material, i.e., the isolated genes have been altered in that they are free of other cellular material.

In view of the foregoing discussion, it is clear that the art with regard to isolation of genes encoding MS which are at least 90% identical to SEQ ID NO:2 and 4 based on the Clustal method of alignment is not unpredictable.

2) State of the Art. The state of the art was developed as evidenced by the above discussion.

3) Number of working examples. Working examples were provided for the MS cDNAs of tobacco, soybean, corn and a partial sequence for wheat.

4) Amount of guidance provided by Applicants. Based on the above-discussion and attached alignment, it is respectfully submitted that Applicants have provided adequate guidance with respect to practicing the claimed invention.

5) Scope of the invention. It is believed that the scope of the claims is commensurate with the breadth of the disclosure.

6) Nature of the invention. The invention concerns an isolated nucleic acid fragment comprising a nucleotide sequence encoding a polypeptide having methionine synthase activity, wherein the amino acid sequence of the polypeptide and the amino acid sequence of SEQ ID NO: 2 or 4 have at least 90% sequence identity based on the Clustal alignment method.

7) Level of skill in the art. The level of skill in the art is high coupled with the predictability of the art, development of the state of the art, scope of the claimed invention, and guidance provided by Applicants, one of ordinary skill in the art would readily be able to practice the claimed invention without engaging in undue experimentation.

Thus, withdrawal of the rejection of the claims under 35 USC §112, first paragraph, on the ground that one skilled in the art would need to engage in undue experimentation in order to make and use the claimed invention is respectfully requested.

Claims 14-25, 29 and 31-33 were rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention on the ground there there is no recitation of the parameter used in the Clustal alignment, specifically, "the metes and bounds of what sequences are included in the claims and what sequences are excluded are unclear."

The Examiner's attention is kindly invited to the claim 14, as amended, and to page 10 of the specification at lines 29-33 which set forth the default parameters for the Clustal alignment method. Given the recitation of parameter, withdrawal of this ground of rejection is respectfully requested.

Withdrawal of this ground of rejection for claims 31-33 is respectfully requested in view of the amendments to claims 31-33.

The rejection of claim 25 has been rendered moot in view of the cancellation of this claim.

It is respectfully submitted that this case is now in form for allowance, which allowance is respectfully solicited.

A petition for a three (3) month extension of time accompanies this response along with Appendix A and copies of the references mentioned herein.

Please charge any fees, or credit any overpayment, which are required in connection herewith including, but not limited to, the filing of this Response and Petition for Extension of Time to Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company).

Respectfully submitted,

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